Embargoed until 6:30 PM EST,
Thursday, Jan. 8, 2004

Contact: Jon Weiner
(323) 442-2830

Air Pollution May Significantly Worsen Respiratory Allergies in Individuals with Genetic Risk

Study in *Lancet* points to how diesel exhaust might trigger more sneezing, coughing

LOS ANGELES (Jan. 8)—As if the sneezing and watery eyes were not bad enough, California researchers have found that airborne components of diesel engine exhaust significantly worsen allergy symptoms in people with a certain genetic makeup.

Researchers from the Keck School of Medicine of the University of Southern California and the David Geffen School of Medicine at UCLA have found that genetic characteristics seen in about half the population leave allergy-sufferers particularly susceptible to the effects of diesel particles. Results appear in the Jan. 10 issue of *Lancet*.

"We've known that diesel exhaust particles worsen symptoms in individuals who respond to allergens, such as pollen, but this study suggests a direct way that pollution could be triggering allergies and asthma in a large number of susceptible individuals, and perhaps a new route of intervention," says Frank D. Gilliland, M.D., Ph.D., professor of preventive medicine at the Keck School and the study's lead author.

Exposure to air pollution is related to numerous health effects, including respiratory allergies. In this study, researchers sought to understand how pollutants from diesel exhaust might cause inflammation in the lungs.

Diesel exhaust particles are thought to act by causing the production of molecules called reactive oxygen species (hydrogen peroxide, for example) in the lungs' airways. In response, the immune system pumps out substances that cause allergy symptoms.

But compounds called antioxidants can detoxify these particles and temper the body's allergic inflammatory response. Researchers suspect that the better the body can use antioxidants to defend itself, the better it can protect itself from airborne pollutants.

With that in mind, researchers investigated a family of antioxidant-related enzymes found in the lungs. Two of these enzymes are called glutathione S-transferase M1, or GSTM1, and glutathione S-transferase P1, or GSTP1. The GSTM1 and GSTP1 genes are

-more-

responsible for creating each of the enzymes, which help the lungs detoxify pollutant products and defuse oxidants before they can cause damage.

GSTM1 occurs in two common forms in the population—either "present" or "null." Differences between present and null forms are small, but they may mean a lot. People born with two of the null form of the gene cannot produce the GSTM1 protective enzyme at all. About 50 percent of the population falls into this category.

Meanwhile, the GSTP1 gene can occur with a common variation called ile105. People born with two of the ile105 form of the gene produce a less-effective form of the GSTP1 enzyme. This less-effective form occurs in about 40 percent of the population.

In this clinical trial, the research team enrolled 19 people with known allergies to ragweed. They sampled participants' DNA to discern which forms of the GSTM1, GSTP1 and other similar genes they had.

Over the next few months, researchers twice gave each participant two treatments: nose spray containing either a dose of ragweed allergen and diesel exhaust particles or spray containing ragweed allergen and a placebo. The amount of diesel particles given was about what someone would experience during 40 hours spent in Southern California.

After administering the spray, researchers measured participants' nasal allergic episodes. They found that participants who lacked the GSTM1 enzyme had a larger allergic response than others. Also, those participants who lacked GSTM1 and had at least one GSTP1 ile105 genetic variant had an even larger allergic response to diesel exhaust particles than did the participants with the other versions of the genes. Researchers estimate that 15 to 20 percent of the population has both genetic variations. This represents a large group especially susceptible to the adverse effects of air pollution.

Further studies are needed to find other genetic variations that may put some at risk for pollution-related lung health problems, and possibly even to cardiovascular events such as heart attacks. Such research may suggest targets for drug interventions.

The work was supported by the Children's Environmental Health Center, which is funded by the National Institute of Environmental Health Sciences (NIEHS) and the Environmental Protection Agency and is based at the Keck School of Medicine. The UCLA Asthma, Allergy and Immunologic Disease Center, which is funded by the National Institute of Allergy and Infectious Diseases, also supported the research. Additional support came from the Southern California Environmental Health Sciences Center, funded by the NIEHS, and the Hastings Foundation.

# # #

Frank D. Gilliland, Yu-Fen Li, Andrew Saxon and David Diaz-Sanchez, "Effect of glutathione-transferase m1 and p1 genotypes on xenobiotic enhancement of allergic responses," *Lancet*. Vol. 363, No. 9403.